PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER		see Form PCT/ISA/220	
P03/252-ve/rg	ACTION as well		as, where applicable, item 5 below.	
International application No.	international filing date (day/month/year)		(Earliest) Priority Date (day/month/year)	
PCT/EP2004/014916	17/11/2004		27/11/2003	
Applicant	<u> </u>			
·				
MERCK PATENT GMBH				
This International Search Report has been according to Article 18. A copy is being tra	n prepared by this international Se ansmitted to the International Bure	arching Aut	nority and is transmitted to the applicant	
This International Search Report consists	of a total ofs	neets.		
It is also accompanied by a copy of each prior art document cited in this report.				
1. Basis of the report a. With regard to the language, the International search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.				
The international this Authority (Ru		s of a transl	ation of the international application furnished to	
b. With regard to any nucle	otide and/or amino acid sequenc	e disclosed	in the International application, see Box No. I.	
2. X Certain claims were fou	nd unsearchable (See Box II).			
3. Unity of invention is lac	king (see Box III).			
4. With regard to the title,				
	ibmitted by the applicant.			
=	shed by this Authority to read as fol	lows:		
_				
5. With regard to the abstract,				
1	approved as submitted by the applicant.			
the text has been establismay, within one month from	shed, according to Rule 38.2(b), by om the date of mailing of this intern	this Author ational seai	ity as it appears in Box No. IV. The applicant rch report, submit comments to this Authority.	
6. With regard to the drawings,				
a. the figure of the drawings to be p	published with the abstract is Figur	9 No	4	
as suggested by				
as selected by th	is Authority, because the applicant	falled to su	ggest a figure.	
as selected by th	is Authority, because this figure be	tter charact	erizes the invention.	
b. none of the figures is to b	e published with the abstract.			

International Application No PCT/EP2004/014916

IPC 7	CO7C211/55 CO7C205/57 CO7C255 CO7C225/10 A61K31/196 A61K31/ A61P3/10 A61P9/10		CO7C317/34 A61K31/166
According to	International Patent Classification (IPC) or to both national classif	cation and IPC	
B. FIELDS		At	
Minimum do IPC 7	cumentation searched (classification system followed by classification ${\tt C07C}$	tion symbols)	
Documentat	ion searched other than minimum documentation to the extent that	such documents are included in the	e fields searched
Electronic da	ata base consulted during the international search (name of data to	pase and, where practical, search ter	rms used)
EPO-In	ternal, CHEM ABS Data, PAJ, BEILSTE	IN Data, WPI Data	
C. DOCUME	ENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the	elevant passages	Relevant to claim No.
X	DATABASE CHEMABS 'Online! CHEMICAL ABSTRACTS SERVICE, COLIOHIO, US; KIZBER, A. I. ET AL: "Transform the series of diazoamino compount Thermal decomposition of carboxy-substituted diazoaminob XP002296498 retrieved from STN Database accession no. 1958:349 abstract & ZHURNAL OBSHCHEI KHIMII, 27 CODEN: ZOKHA4; ISSN: 0044-460X,	ations in nds. I. enzenes" 14 , 2208-13	1-4
X Fur	ther documents are listed in the continuation of box C.	Patent family members a	are listed in annex.
 Special categories of cited documents: 'A' document defining the general state of the art which is not considered to be of particular relevance 'E' earlier document but published on or after the international filing date 'L' document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) 'C' document referring to an oral disclosure, use, exhibition or other means 'P' document published prior to the international filing date but later than the priority date calmed 'T' later document published after the international or priority date and not in conflict with cited to understand the principle or the inventional invention involve an inv		ance; the claimed invention or cannot be considered to hen the document is taken alone ance; the claimed invention or cannot be considered to hen the document is taken alone ance; the claimed invention volve an inventive step when the one or more other such docueing obvious to a person skilled	
	actual completion of the International search	Date of mailing of the interna	ational search report
	17 May 2005	22/06/2005	
Name and	mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Bedel, C	

4

International Application No PCT/EP2004/014916

ation) DOCUMENTS CONSIDERED TO BE RELEVANT	Relevant to claim No.
Citation of document, with indication, where appropriate, of the relevant passages	Helevant to claim No.
KNOCHEL PAUL: "A New General Preparation of Polyfunctional Diarylamines by the Addition of Functionalized Arylmagnesium Compounds to Nitroarenes" J.AM.CHEM.SOC., no. 124, 2002, pages 9390-9391, XP002296494 page 9391; example 1d; table 1	1-5
PATENT ABSTRACTS OF JAPAN vol. 0070, no. 19 (C-147), 25 January 1983 (1983-01-25) & JP 57 175106 A (YOSHIO KATSUTA), 28 October 1982 (1982-10-28) voir aussi dans le brevet p.43 dans le tableau les exemples 3,4,8 et 11, les substituants R et Y. abstract	1-5
US 4 316 044 A (ISHIMITSU KEIICHI ET AL) 16 February 1982 (1982-02-16) examples	1-4
GB 1 307 284 A (BOOTS PURE DRUG CO LTD) 14 February 1973 (1973-02-14) page 4, line 4 - page 5, line 2; claim 1 page 8, line 10 - line 18 page 9, line 10 - line 34	1-4,6-8
PATENT ABSTRACTS OF JAPAN vol. 0165, no. 66 (C-1009), 8 December 1992 (1992-12-08) & JP 04 220442 A (SUMITOMO CHEM CO LTD), 11 August 1992 (1992-08-11) see also examples abstract	1-3
US 5 196 610 A (CARR ROBIN A E ET AL) 23 March 1993 (1993-03-23) column 44, line 39 - column 45, line 28; example 36	1-4
WO 03/087045 A (LITTLE PAUL BRIAN; RECEVEUR JEAN-MARIE (DK); ULVEN TROND (DK); 7TM PH) 23 October 2003 (2003-10-23) voir les réactifs utilisés page 79; examples 90-92	1-4
WO 03/076406 A (MERCK PATENT GMBH) 18 September 2003 (2003-09-18) page 26, line 1 - line 23 page 29, line 5 - page 30, line 2; table C	6-14
	of Polyfunctional Diarylamines by the Addition of Functionalized Arylmagnesium Compounds to Nitroarenes" J.AM.CHEM.SOC., no. 124, 2002, pages 9390-9391, XP002296494 page 9391; example 1d; table 1 PATENT ABSTRACTS OF JAPAN vol. 0070, no. 19 (C-147), 25 January 1983 (1983-01-25) & JP 57 175106 A (YOSHIO KATSUTA), 28 October 1982 (1982-10-28) voir aussi dans le brevet p.43 dans le tableau les exemples 3,4,8 et 11, les substituants R et Y. abstract US 4 316 044 A (ISHIMITSU KEIICHI ET AL) 16 February 1982 (1982-02-16) examples GB 1 307 284 A (BOOTS PURE DRUG CO LTD) 14 February 1973 (1973-02-14) page 4, line 4 - page 5, line 2; claim 1 page 8, line 10 - line 18 page 9, line 10 - line 34 PATENT ABSTRACTS OF JAPAN vol. 0165, no. 66 (C-1009), 8 December 1992 (1992-12-08) & JP 04 220442 A (SUMITOMO CHEM CO LTD), 11 August 1992 (1992-12-08) & JP 04 220442 A (SUMITOMO CHEM CO LTD), 11 August 1992 (1992-08-11) see also examples abstract US 5 196 610 A (CARR ROBIN A E ET AL) 23 March 1993 (1993-03-23) column 44, line 39 - column 45, line 28; example 36 WO 03/087045 A (LITTLE PAUL BRIAN; RECEVEUR JEAN-MARIE (DK); ULVEN TROND (DK); 7TM PH) 23 October 2003 (2003-10-23) voir les réactifs utilisés page 79; examples 90-92 WO 03/076406 A (MERCK PATENT GMBH) 18 September 2003 (2003-09-18) page 26, line 1 - line 23 page 29, line 5 - page 30, line 2; table C

4

International Application No
PCT/EP2004/014916

Category °	ation) DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	PETER J. O'BRIEN: "A comparison of hepatocyte cytotoxic mechanisms for Cu2+ and Cd2+" TOXYCOLOGY, no. 143, 2000, pages 263-273, XP002296495 table 1 page 269, left-hand column, paragraph 2	6-14
A	GÖNÜL SAHIN: "Effects of some probable antioxidants on the selenite-induced cataract formation and oxidative stres-related paramaters in rats" TOXYCOLOGY, no. 139, 1999, pages 219-232, XP002296496 page 220, left-hand column, paragraph 2 page 223; tables 1,2	6-14
Α .	JEFFERY W. KELLY: "Synthesis, Structure and Activity of Diclofenac Analogues as Transthyretin Amyloid Fibril Formation Inhibitors" J.MED.CHEM., no. 45, 2002, pages 321-332, XP002296497 page 325; table 2	6-14
X	DATABASE BEILSTEIN BEILSTEIN INSTITUTE FOR ORGANIC CHEMISTRY, FRANKFURT-MAIN, DE; XP002328213 Database accession no. 5061244 abstract & GORVIN, JOHN H.: J.CHEM.SOC.PERKIN TRANS.1, 1988, pages 1331-1336,	5
А	DATABASE BEILSTEIN BEILSTEIN INSTITUTE FOR ORGANIC CHEMISTRY, FRANKFURT-MAIN, DE; XP002328214 Database accession no. 2813438 abstract & LANTZ: BULL.SOC.CHIM.FR., 1956, pages 311-315,	5
X	DATABASE CA CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; WARD YANCEY D.: "Solid phase synthesis of aryl amines via palladium catalysed amination of resin-bound aromatic bromides" XP002328215 Database accession no. 1996:605697 abstract & TETRAHEDRON LETTERS, vol. 37, no. 39, 1996, pages 6993-6996,	5
	-/	

International Application No
PCT/EP2004/014916

ategory °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
ζ	DATABASE CA CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; BURGER ALFRED: "Some derivatives of 4'-hydroxydiphenylamine-4-carboxylic acid" XP002328216 Database accession no. 1956:44350 abstract & J.A.C.S., no. 77, 1955, page 5733,	5
1	MAFFEI FACINO R ET AL: "ANTIOXIDANT PROFILE OF NIMESULIDE, INDOMETHACIN AND DICLOFENAC IN PHOSPHATIDYLCHOLINE LIPOSOMES (PCL) AS MEMBRANE MODEL" INTERNATIONAL JOURNAL OF TISSUE REACTIONS, BIOSCIENCE EDIPRINT, GENEVA, CH, vol. 15, no. 6, 1993, pages 225-234, XP002048767 ISSN: 0250-0868 the whole document	6-14

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 1-4, 6 (partially)

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of the claim(s) may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claim(s) is impossible. Consequently, the search has been restricted to:
A combination of claims 3-4 as well as claim 5 and a combination of claims 7-9 as well as claim 10.

The use of these compounds as antioxydants has been searched on the full scope of formula (II) (cl.11-14)

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

International application No. PCT/EP2004/014916

INTERNATIONAL SEARCH REPORT

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)	
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:	
Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:	
2. X Claims Nos.: 1-4, 6 (partially) because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:	
see FURTHER INFORMATION sheet PCT/ISA/210	
3. Claims Nos.:	
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).	
Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)	
This International Searching Authority found multiple inventions in this international application, as follows:	
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.	
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.	
3. As only some of the required additional search fees were timely paid by the applicant, this international Search Report covers only those claims for which fees were paid, specifically claims Nos.:	
4. No required additional search fees were timely paid by the applicant. Consequently, this international Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:	
Remark on Protest The additional search fees were accompanied by the applicant's protest.	
No protest accompanied the payment of additional search fees.	